REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. With entry of this amendment, claims 1, 3, 5, 7, 9, 11, 13, 15, and 17 will be pending and claims 2, 4, 6, 8, 10, 12, 14, 16 and 18-20 will be cancelled. Support for the amendment to claim 1 is found, *inter alia*, at pages 10, lines 2-3 from the bottom for (a) and page 7, fourth paragraph for (c).

Rejections Under 35 U.S.C. § 102(b)

Former claims 1, 3-6, 9, 11-14 and 17 were rejected under 35 U.S.C. § 102(b) as being anticipated by Dmitriev *et al.* (Journal of Virology, 1998). As recited in amended claim 1, the present invention disclose a method for constructing a fiber-mutant adenovirus vector wherein an oligonucleotide containing a foreign peptide-coding DNA is introduced directly into a fiber HI loop-coding region of the plasmid that has a complete adenovirus genome, except for the E1 and E3 regions. The present invention allows the introduction of the oligonucleotide containing the foreign peptide-coding DNA into the fiber HI loop-coding sequence in only one step by the following. An insertion of a *Csp*45I and/or *Cla*I recognition sequence into the fiber HI loop-coding gene sequence of the plasmid to which the complete adenovirus genome except E1 and E3 is incorporated and a preparation of an oligonucleotide sequence designed so as to bind with the *Csp*45 and/or *Cla*I recognition sequence.

In contrast, the oligonucleotide containing the foreign peptide-coding DNA cannot be introduced directly into the adenovirus genome in Dmitriev *et al.* In Dmitriev *et al.*, a modified fiber is firstly prepared by inserting a foreign peptide-coding DNA into the EcoRV site in the plasmid to which a fiber HI loop-coding region (not complete adenovirus genome) is subcloned. Next, the modified fiber is cut out from the plasmid and introduced into the adenovirus genome by homologous recombination using a special strain of Escherichia coli (BJ5 183). Then, the prepared plasmid is re-transformed with normal strain of Escherichia coli (e.g. DH5α), because the plasmid in BJ5183 is too unstable. Though Dmitriev et al. introduce a unique *Swa*I site into the adenovirus genome, the *Swa*I site is used only for cleaving the fiber region when introducing modified fiber into the adenovirus genome by homologous recombination. Since there was originally no idea in Dmitriev *et al.* regarding an

introduction using the restriction enzyme recognition sequence, the oligonucleotide to be introduced is not prepared to bind with the *Swa*I site. Moreover, even if the oligonucleotide were prepared to bind with the *Swa*I site, it is too difficult to introduce it directly into the adenovirus genome because the *Swa*I-treated end is blunt, in instances where the size of the plasmid is large (for example, 30 kb or more). Also, the *Swa*I site is not introduced into a fiber HI loop-coding region in their method. The *Swa*I site is introduced into a fiber tail region-coding region. Therefore, Dmitriev *et al.* require a complicated and time-consuming homologous recombination method.

Rejections Under 35 U.S.C. § 103

Former claims 1-18 were rejected under 35 U.S.C. § 103 as being anticipated by Dmitriev *et al.* (Journal of Virology, 1998) in view of Arap *et al.* (Science, 1998). Prior to the present invention, there was no suggestion or motivation of trying to construct fiber-mutant adenovirus using techniques other than homologous recombination at the time of the priority date of the present invention. The cited references (Dmitriev *et al.* and Arap *et al.*) do not disclose or suggest a technique for introducing oligonucleotide directly into the fiber HI loop-coding gene sequence of the plasmid to which total adenovirus genome except E1 and E3 regions is incorporated without the subcloning of one part of the fiber, as in the present invention. Thus, the present invention is not suggested or motivated by the cited references.

In addition, the present invention requires only one step for introducing the oligonucleotide containing the foreign peptide-coding DNA, whereas Dmitriev *et al.* requires several steps (preparation of a modified fiber using another vector to which one part of the fiber is subcloned, homologous recombination, and re-transformation). That is, it takes only two days to prepare the mutant adenovirus vector in the present invention, whereas it takes at least 8 to 10 days to prepare it in Dmitriev *et al.* As such, the procedure of constructing fiber mutant adenovirus has been remarkably improved and simplified by the present invention. Such remarkable effects could not have been reasonably expected by any combination of the cited references.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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